Cardiac surgery and the kidney
– studies on the effects of pharmacological interventions on renal perfusion, filtration and oxygenation

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Gudrun Bragadottir
Leg. läkare

Fakultetsopponent
Docent Claes-Roland Martling
Avdelningen för Fysiologi och Farmakologi
Sektionen för Anestesiologi och Intensivvård
Karolinska Institutet, Solna

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I. Bragadottir G, Redfors B, Nygren A, Sellgren J, Ricksten SE
Low-dose vasopressin increases glomerular filtration rate, but impairs renal oxygenation in post-cardiac surgery patients.
Acta Anaesthesiol Scand 2009; 53: 1052 -1059

II. Bragadottir G, Redfors B, Ricksten SE
Mannitol increases renal blood flow and maintains filtration fraction and oxygenation in postoperative acute kidney injury; a prospective interventional study.
Crit Care 2012; Aug17;16(4):R159

III. Bragadottir G, Redfors B, Ricksten SE
Effects of levosimendan on glomerular filtration rate and renal blood flow and renal oxygenation after cardiac surgery with cardiopulmonary bypass - a randomized placebo-controlled study.
Accepted for publication in Critical Care Medicine

IV. Bragadottir G, Redfors B, Ricksten SE
Assessing glomerular filtration rate (GFR) in critically ill patients with acute kidney injury (AKI) - true GFR versus urinary creatinine clearance and estimating equations.
Manuscript submitted

UNIVERSITY OF GOTHENBURG

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Gudrun Bragadottir

Department of Anaesthesiology and Intensive Care, Institute of Clinical Sciences, The Sahlgrenska Academy, University of Gothenburg, Sweden

Abstract

Acute kidney injury (AKI) commonly complicates cardiac surgery and is associated with high mortality. Renal ischemia is considered to be the major cause. There is a close association between glomerular filtration rate (GFR), tubular sodium reabsorption and renal oxygen consumption (RVO_2) in humans. The filtered load of sodium is an important determinant of RVO_2 and any agent that increases GFR has the potential to increase RVO_2. An ideal agent to treat patients with AKI would be one that increases both renal blood flow (RBF) and GFR, with no impairment in renal oxygenation, defined as the renal oxygen supply/demand relationship, the inverse of this relationship being the renal extraction of O_2 (RO_2Ex). Data on the effects of pharmacological interventions on RBF, GFR and renal oxygenation, are scarce.

Patients and methods: The renal vein thermodilution technique was used to analyse the effects of vasopressin (n=12) and the effects of levosimendan vs placebo (n=30), on RBF, GFR and renal oxygenation in post-cardiac surgery patients. The effects of mannitol on RBF, GFR and renal oxygenation were studied in patients (n=11) with AKI after cardiac surgery. The agreement of urinary creatinine clearance (CrCl) and three commonly used estimating equations, in comparison to GFR, measured by the infusion clearance of ^{51}Cr-EDTA, were evaluated in critically ill patients with AKI.

Results: Vasopressin increased renal vascular resistance (RVR) and decreased RBF, while GFR, RVO_2 and RO_2Ex increased. Mannitol in AKI, increased urine flow, decreased RVR and increased RBF. Mannitol tended to increase GFR and RVO_2 but did not change RO_2Ex. Compared to placebo, levosimendan decreased RVR and increased RBF and GFR, while RVO_2 and RO_2Ex were not affected. Finally, the within-group error was higher for the urinary CrCl method than the ^{51}Cr-EDTA clearance method. The urinary CrCl method and the estimating equations had high biases and high errors compared to GFR measured by ^{51}Cr-EDTA.

Conclusion: The vasopressin-induced increase in GFR was caused by post-glomerular renal vasoconstriction, accompanied by an increase in RVO_2 and RO_2Ex. Thus, vasopressin impaired renal oxygenation. Mannitol treatment of AKI induced a renal vasodilation and increased RBF. Mannitol did neither affect filtration fraction nor renal oxygenation, suggestive of balanced increases in perfusion/filtration and oxygen demand/supply. Levosimendan induced a vasodilation, preferentially of pre-glomerular resistance vessels, increasing both RBF and GFR without jeopardizing renal oxygenation. Levosimendan could therefore be a potentially useful agent for treatment of AKI in patients with heart failure. Assessment of GFR by the urinary CrCl method, had a poor precision in critically ill patients with AKI, and should not be used as a reference method, when validating new methods for assessing kidney function in this patient population. All the estimating equations performed poorly, when estimating GFR in these patients.

Key words: Kidney failure, acute; glomerular filtration rate; renal circulation; oxygen consumption; cardiac surgery; vasopressin; mannitol; levosimendan; estimating equations.
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